1. Document ID: US 6177075 B1

L8: Entry 1 of 18
File: USPT
Jan 23, 2001

US-PAT-NO: 6177075
DOCUMENT-IDENTIFIER: US 6177075 B1
TITLE: Insect viruses and their uses in protecting plants
DATE-ISSUED: January 23, 2001

US-CL-CURRENT: 424/93.2; 424/93.6, 435/235.1

APPL-NO: 8/ 485355
DATE FILED: June 7, 1995

PARENT-CASE:
This is a continuation-in-part of U.S. application Ser. No. 08/440,522, filed May 12, 1995,
abandoned, which is a continuation-in-part of U.S. application Ser. No. 08/089,372, filed Jul. 9,
1993, abandoned, which is a convention application of Australian Patent.--Application PL4081/92,
filed Aug. 14, 1992.

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY
APPL-NO
APPL-DATE
AU
PL4081/92
August 14, 1992

IN: Christian; Peter Daniel, Gordon; Karl Hienrich Julius, Hanzlik; Terry Nelson

AB: The present invention relates to an isolated small RNA virus capable of infecting
insect species including Heliothis species, and to the nucleotide sequences and proteins
encoded thereby. The invention contemplates uses of the virus in controlling insect attack
in plants.

L8: Entry 1 of 18
File: USPT
Jan 23, 2001

DOCUMENT-IDENTIFIER: US 6177075 B1
TITLE: Insect viruses and their uses in protecting plants

DEPV:
It is the activity of the HaSV replicase and not virosis or accumulation of viruses that causes
the midgut cell to cease functioning. This is shown by data generated from the following
experiment. When protoplasts are transfected with genes that make a replicatable RNA1 and only
the capsid protein and not a replicatable RNA2 (R1-HC and VCAPB according to procedures listed
above), stunting occurs. When the stunted larvae are extracted for RNA which is then northern
blotted with probe for HaSV nucleic acid, only RNA1 of HaSV is seen to be present. Stunting does
not occur when the protoplasts are transfected with genes that do not make a replicatable RNA1
(lacking an effective ribozyme to cleave after the last viral base in the gene) and only the
capsid protein and not a replicatable RNA2 (R1-HDV and VCAPB according to procedures listed
elsewhere in patent). When the stunted larvae are extracted for RNA which is then northern
blotted with probe for HaSV nucleic acid, no HaSV RNA is seen to be present.

2. Document ID: US 6120803 A

L8: Entry 2 of 18
File: USPT
Sep 19, 2000

US-PAT-NO: 6120803
DOCUMENT-IDENTIFIER: US 6120803 A
TITLE: Prolonged release active agent dosage form adapted for gastric retention
DATE-ISSUED: September 19, 2000

US-CL-CURRENT: 424/473; 424/468, 424/469, 424/470, 424/486, 424/488, 514/772.2, 514/772.3,
514/777, 514/778, 514/781, 514/782, 514/784

APPL-NO: 9/ 131923
DATE FILED: August 10, 1998

PARENT-CASE:
This application claims the priority of provisional application Ser. No. 60/055,475, filed Aug.
11, 1997, which is incorporated herein by reference .

IN: Wong; Patrick S. L., Dong; Liang-Chang, Edgren; David E., Theeuwes; Felix,
Gardner; Phyllis I., Jao; Francisco, Wan; Jason J.

AB: The present invention is directed to an active agent dosage form which is adapted
for retention in the stomach and useful for the prolonged delivery of an active agent
formulation to a fluid environment of use. The active agent dosage form is a polymer matrix
that swells upon contact with the fluids of the stomach. A portion of the polymer matrix is
surrounded by a band of insoluble material that prevents the covered portion of the polymer
matrix from swelling and provides a segment of the dosage form that is of sufficient
rigidity to withstand the contractions of the stomach and delay expulsion of the dosage form
from the stomach until substantially all of the active agent has been dispensed.

L8: Entry 2 of 18
File: USPT
Sep 19, 2000

DOCUMENT-IDENTIFIER: US 6120803 A
TITLE: Prolonged release active agent dosage form adapted for gastric retention

DEPR:
The present invention is particularly useful to deliver active agents that are poorly absorbed in
the lower gastrointestinal tract, but well absorbed in the upper gastrointestinal tract (i.e.,
the small intestine) or active agents that exhibit poor solubility such that the increased
retention time in the stomach allows for a greater quantity of active agent to dissolve from the
dosage form than would otherwise be dissolved. Typically, antiviral, antifungal and antibiotic

agents, e.g. sulfonamides, quinolones, penicillins, cephalosporins, aminoglycosides, and
tetracyclines, are representative classes of agents for which the invention is particularly
useful. Such antibiotic agents may include, for example, .beta.-lactam antibiotics, vancomycin,
clidamycin, erthromycin, trimethoprim-sulfamethoxaazole, rifampin, ciprofloxacin, amoxicillin,
clindamycin, ceftriaxone, cefotaxime, chloramphenicol, clindamycin, cefoxitin, doxyclycline,
spectinomycin, ofloxacin, rifampin, minocycline, doxycycline, aztreonam, imipenem, meropenem,
nitrofurantoin, azithromycin, atovaquone, trimetrexate, dapsone, primaquin, trimetrexate,
ketoconazole, floconazole, amphotericin B, itraconazole, trifluridine, foscarnet, zidovudine
amantadine, interferon alfa, sulfonamides such as sulfisoxazole, sulfadiazine, and sulfasalazine,
quinolones and fluoroquinolones such as, for example, cinoxacin, forfloxacin, diprofloxacin,
ofloxacin, spardlosxacin, lomefloxacin, fleroxacin, pefloxacin and amifloxacin, gentamicin,
tobramycin, amikacin,netilmicin, kanamycin,and neomycin. Representative antiviral agents include
acyclovir, famciclovir, foscarnet, ganciclovir, idoxuridine, sorivudine, trifluridine,
valacylcovir, vidarabine, didanosine, stavudine, zalcitabine, zidovudine, amantadine,
interferons, e.g., interfon alpha, ribavirin, rimantadine, nucleoside RT inhibitors, such as
lamivudine and adeforvir, non-nucleoside inhibitors such as nevrapine, delavairidine, Iviride,
saquinavir and indinavir, nucleoside DNAp inhibitors such as famciclovir, fialuridine, cidofovir
and lobucavir, antisense oligonucleotides such as afovirsen, receptor decoys such as sICAM-1,
capsid binding agents such as pirodavir, and neuraminidase inhibitors such as GG167.

3. Document ID: US 6107028 A

L8: Entry 3 of 18

File: USPT

Aug 22, 2000

US-PAT-NO: 6107028
DOCUMENT-IDENTIFIER: US 6107028 A
TITLE: Ribozymes for treating hepatitis C
DATE-ISSUED: August 22, 2000

US-CL-CURRENT: 435/6; 435/320.1, 435/366, 435/370, 435/91.31, 536/23.1, 536/24.5

APPL-NO: 8/ 648272
DATE FILED: May 15, 1996

PARENT-CASE:
This application is a continuation-in-part of U.S. Ser. No. 08/534,220 filed Sep. 11, 1995, which
is a continuation-in-part of U.S. Ser. No. 08/476,257, filed Jun. 7, 1995, now abandoned, which
is a continuation-in-part of U.S. Ser. No. 08/357,508, filed Dec. 14, 1994, now abandoned. The
contents of all such related applications are incorporated herein by reference in their entirety.

IN: Kay; Mark A., Lieber; Andre

AB: A method of inhibiting hepatitis C virus RNA replication or expression is
provided. The method consists of introducing two or more ribozymes specific for hepatitis C
virus RNA into a cell infected with hepatitis C virus. The ribozymes specific for hepatitis
C virus RNA can specifically cleave hepatitis C RNA in a HCV 5' non-coding sequence, the
capsid sequence, the NS-5 sequence or any other conserved region of the hepatitis C RNA. The
ribozymes can also be selected so as to be specific for opposite strands of the virus
genome. A method of inhibiting hepatitis C virus RNA replication or expression is also
provided which consists of introducing into a cell infected with hepatitis C virus at least
one ribozyme specific for hepatitis C virus which is selected from the group consisting of
GGGAGGTCTCGTAGA [SEQ ID NO: 1], GCACCATGAGCACGA [SEQ ID NO: 2], CCCACAGGACGTCAA [SEQ ID NO:
3], CAACCGTCGCCCACA [SEQ ID NO: 4], TAAACCTCAAAGAAA [SEQ ID NO: 5] GTAAGGTCATCGATA [SEQ ID
NO: 6]. Compositions consisting of two or more ribozymes specific for hepatitis C virus RNA
is also provided.

L8: Entry 3 of 18

File: USPT

Aug 22, 2000

DOCUMENT-IDENTIFIER: US 6107028 A
TITLE: Ribozymes for treating hepatitis C

BSPR:
In another aspect the methods comprise transducing cells, especially hepatocytes, with a
recombinant adenovirus which encodes a ribozyme specific for hepatitis C virus RNA. When the
sequence encoding the ribozyme is expressed, HCV RNA in the infected cell is inhibited or
infection is prevented. Preferably the ribozyme is a hammerhead ribozyme, and specifically
cleaves hepatitis C RNA in a HCV 5' non-coding sequence, capsid sequence, the NS-5 sequence or
any other conserved region of the hepatitis C RNA. Administration may be performed with
hepatocytes from an HCV-infected individual, i.e., ex vivo administration, or administered to the
individual. When administered to an individual, typically administration will be by infusion,
such as via the portal vein or bile duct. Typically the recombinant adenovirus is administered to
the hepatocytes in an amount and for a time sufficient to eradicate hepatitis C virus from the
hepatocytes, preferably from about 10 to 100 adenovirus particles per hepatocyte. For increased
activity against HCV, the vector(s) may encode two or more ribozymes specific for different
regions or strands of HCV RNA.

DEPR:
As mentioned above, the HCV RNA target region is typically one that is substantially conserved
among the prevalent strains of HCV. These regions include the 5' noncoding region, the capsid
protein, and the nonstructural proteins NS-2, NS-3 (helicase), NS-4, NS-5 (RNA polymerase), and
conserved regions of E1 (gp30) and NS-1 (gp72), for example. Representative examples of HCV
ribozyme target sequences include, for HCV types 1a and 1b (where putative cleave sites are
indicated by a "-"), ribozyme 1 (Rz1): GGGAGGTCTCGTAGA [SEQ ID NO: 1] (5' NTR, nucleotides 318 to
332; plus strand), Rz2: GCACCATGAGAGCACGA [SEQ ID NO: 2] (nucleotide 335 to 349; minus strand),
Rz3: CCCACAGGACGTCAA [SEQ ID NO: 3] (capsid, nucleotide 395 to 409; minus strand), Rz4:

CAACCGTCGCCCACA [SEQ ID NO: 4] (capsid, nucleotide 386 to 400; plus strand), Rz5: TAAACCTCAAAGAAA
[SEQ ID NO: 5] (capsid, nucleotide 358 to 370; plus strand), and Rz6: GTAAGGTCATCGATA [SEQ ID NO:
6] (capsid, nucleotide 699 to 714; plus strand).

DEPR:
FIG. 2 shows cleavage sites for these six HCV ribozymes, designated Rz1-Rz6, on the HCV RNA plus
and minus strands. The HCV ribozyme target sequences are as follows, based on a CDNA sequence
that corresponds to the HCV type 1a and type 1b RNA, where the putative ribozyme cleavage sites
are indicated by a "-": ribozyme 1 (Rz1): GGGAGGTCTCGTAGA [SEQ ID NO: 1] (5' NTR, nucleotides 318
to 332; plus strand), Rz2: GCACCATGAGCACGA [SEQ ID NO: 2] (nucleotide 335 to 349; minus strand),
Rz3: CCCACAGGAGTCAA [SEQ ID NO: 3] (capsid, nucleotide 395 to 409; minus strand), Rz4:
CAACCGTCGCCCACA [SEQ ID NO: 4] (capsid, nucleotide 386 to 400; plus strand), Rz5: TAAACCTCAAAGAAA
[SEQ ID NO: 3] (capsid, nucleotide 358 to 370; plus strand), and Rz6: GTAAGGTCATCGATA [SEQ ID NO:
6] (capsid, nucleotide 699 to 714; plus strand). In summary, the four ribozymes designated Rz 1,
4, 5, 6 cleaved the HCV plus RNA at positions 325, 393, 363, 707, respectively and ribozymes
designated Rz 2 and 3 cleaved the minus strand at positions 342 and 401, respectively.

CLPR:
6. The method claim 1, wherein a second ribozyme of said two or more ribozymes specific for
hepatitis C virus RNA specifically cleaves hepatitis C virus RNA in a HCV 5' non-coding sequence,
the capsid sequence, or NS-5 sequence.

CLPR:
17. The composition of claim 15, wherein a second ribozyme of said two or more ribozymes specific
for hepatitis C virus RNA specifically cleaves hepatitis C virus RNA in a HCV 5' non-coding
sequence, the capsid sequence, or NS-5 sequence.

CLPR:
27. The method claim 22, wherein a second ribozyme of said two or more ribozymes specific for
hepatitis C virus RNA specifically cleaves hepatitis C virus RNA in a HCV 5' non-coding sequence,
the capsid sequence, or NS-5 sequence.

4. Document ID: US 6107062 A

L8: Entry 4 of 18
File: USPT
Aug 22, 2000

US-PAT-NO: 6107062
DOCUMENT-IDENTIFIER: US 6107062 A
TITLE: Antisense viruses and antisense-ribozyme viruses
DATE-ISSUED: August 22, 2000

US-CL-CURRENT: 435/91.41; 435/235.1, 435/236, 435/320.1, 435/456, 536/23.1, 536/23.72, 536/24.5

APPL-NO: 7/921104
DATE FILED: July 30, 1992

IN: Hu; Wen, Wang; Jie

AB: Antisense viruses and antisense ribozyme viruses are disclosed. The novel
artificial viruses, their synthesis and their use in preventing and treating viral
infections are presented.

L8: Entry 4 of 18
File: USPT
Aug 22, 2000

DOCUMENT-IDENTIFIER: US 6107062 A
TITLE: Antisense viruses and antisense-ribozyme viruses

DEPR:
The antisense virus of the invention comprises the viral coat (i.e., the envelope and optionally
the capsid in the case of enveloped viruses, and the capsid in the case of viruses without an
external envelope) sufficiently duplicative of a naturally occurring viral coat to give the
antisense virus the infectivity of the naturally occurring virus, and nucleic acid including an
antisense fragment which is antisense to a section of a gene encoding a transactivating protein
required for said naturally occurring virus to replicate. The antisense fragment encodes
antisense RNA which is capable of binding and inactivating mRNA encoded by the gene encoding a
transactivating protein. Typically, the viral coat of the antisense virus is identical to the
corresponding naturally occurring virus. The nucleic acid of the antisense virus typically
contains all the structural genes of the naturally occurring virus. Further, nucleic acid
typically includes all of the regulatory genes of the naturally occurring virus except the gene
encoding the transactivating protein. Advantageously, the nucleic acid of the antisense virus is
the same as the nucleic acid of the corresponding virus with the exception of the antisense
fragment (which replaces a section of a gene). Since the antisense virus does not contain a gene
required for replication of the virus, the antisense virus is replication defective. The
antisense fragment is part or all of the gene encoding the protein required for replication,
turned antisense. The length of the antisense fragment must be sufficient to permit the antisense
RNA transcribed from the antisense fragment to bind and inactivate the mRNA encoded by the gene
encoding the required protein of the naturally occurring virus, thus thwarting replication of the
naturally occurring virus. Thus, the antisense fragment is part or all of the target gene turned
antisense. As used herein, the term "section of a gene" refers to part or all of the gene(s)
encoding the transactivating protein(s) required for the naturally occurring virus to replicate.

5. Document ID: US 6043077 A

L8: Entry 5 of 18
File: USPT
Mar 28, 2000

US-PAT-NO: 6043077
DOCUMENT-IDENTIFIER: US 6043077 A
TITLE: Hepatitis C virus ribozymes

DATE-ISSUED: March 28, 2000

US-CL-CURRENT: 435/236; 435/320.1, 435/325, 435/363, 435/366, 435/375, 435/6, 435/91.31, 536/23.1, 536/23.2, 536/24.1, 536/24.5

APPL-NO: 8/ 954210
DATE FILED: October 20, 1997

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATION This application is a continuation-in-part of U.S. application Ser. No. 08/608,862, filed Feb. 29, 1996 now abandoned; and claims priority under 35 U.S.C. .sctn..sctn. 119/365 from pending PCT Application No. PCT/US97/03304, filed Feb. 27, 1997, which applications are incorporated by reference in their entirety.

IN: Barber; Jack R., Welch; Peter J., Tritz; Richard, Yei; SoonPin, Yu; Mang

AB: This invention provides ribozymes useful to treat or prevent Hepatitis C Virus ("HCV") infection or disease in an organism or subject, as well as methods of treating an HCV infection or disease. Reagents such as vectors, host cells, DNA molecules coding for these ribozymes useful in methods of treatment and prevention of HCV infection or disease are also provided.

L8: Entry 5 of 18

File: USPT

Mar 28, 2000

DOCUMENT-IDENTIFIER: US 6043077 A
TITLE: Hepatitis C virus ribozymes

DRPR:
FIG. 7 shows in vitro cleavage reactions using variants of CR4 ribozyme with either 8, 7 or 6 nucleotides in Helix 1, using the short capsid substrate.

DRPR:
FIG. 8 depicts in vitro cleavage reactions using variants of CR4 ribozyme with either 8, 7 or 6 nucleotides in Helix 1 using the long capsid substrate.

DEPR:
HCV hairpin ribozymes can be applied to the detection and diagnosis of HCV infection. To accomplish this, a special reporter plasmid is generated which contains the HCV 5'-capsid sequence upstream of the E. coli lacZ gene (nucleotides 1302-4358, Genbank accession no. J01636). This plasmid is made via a two-step cloning process. First, HCV sequences containing the 5' UTR and capsid coding region are synthesized directly from RNA that was extracted from an HCV-positive patient serum sample. The purified viral RNA is then reverse transcribed and PCR amplified with the following primers: sense (starting at 5' end of 5' UTR) 5'-GCCAGCCCCC TGATGGGG-3' (Sequence ID No. 6) and antisense (starting at 3' end of capsid coding region) 5'-CACCTGATAA GCGGAAGC-3' (Sequence ID No. 7). The resulting blunt-end DNA is then ligated the unique Sma I site in pCMV.beta. (Clontech, Palo Alto, Calif.). This first generation plasmid is designated pCMV-HCV-.beta.. Second, to allow selection of this plasmid following transfection into mammalian cells, a neomycin resistance expression cassette, consisting of the SV40 early promoter driving the expression of the neomycin resistance gene, is constructed. This is accomplished by blunt-ligating a BamHI fragment, containing the neomycin cassette obtained from pMAMneo-LUC (Clontech, Palo Alto, Calif.), into the unique SalI site of pCMV-HCV-.beta.. The resulting plasmid, pCMV-HCV-.beta.-SV-neo expresses two independent RNAs. One containing the HCV target sites upstream of the lacZ coding sequence, and the other expressing neomycin resistance for positive selection.

DEPR:
To generate the reporter cell line, the human hepatocellular carcinoma cell line Huh7 (Yoo et al., J. Virol. 69:32-38, 1995), is co-transfected with pCMV-HCV-.beta.-SV-neo and an HCV hairpin ribozyme expression plasmid, pLNT-Rz. G418-selected transfected Huh7 cells, containing both Rz and reporter plasmids, is then used for HCV infection diagnosis. Under normal conditions, expressed HCV Rz will cleave the HCV 5'UTR-capsid target located on the lacZ mRNA, resulting in the inhibition of .beta.-galactosidase expression. When cells are challenged with a biological sample (e g., patient serum samples or other blood products containing HCV, or tissue or cell samples taken from the liver), the presence of the HCV 5'UTR-capsid sequences coming from the replicating HCV will compete for the ribozyme, interfering with its ability to cleave the HCV-lacZ RNA. The result of this interference in Rz activity is an increased expression of .beta.-galactosidase and these cells will stain blue by routine lacZ staining. Thus, any patient serum (or other biological sample) which is positive for hepatitis C virus will cause these reporter cells to turn blue.

DEPR:
Construction of several expression vectors is described herein (FIG. 9). The HCV reporter plasmid pPur-HCV (FIG. 9B) is constructed as follows: HCV sequences containing the 5'UTR and capsid coding region are synthesized directly from RNA that is extracted from an HCV-positive patient serum sample. The purified viral RNA is then reverse transcribed and PCR amplified with the following primers: sense (starting at 5' end of 5' UTR) 5'-GCCAGCCCCC TGATGGGG-3' (Sequence ID No. 6) and antisense (starting at 3' end of capsid coding region) 5'-CACCTGATAA GCGGAAGC-3' (Sequence ID No. 7). The resulting blunt-end DNA is then ligated into plasmid pPur (Clontech, Palo Alto, Calif.; FIG. 9A) that has been digested with XbaI and blunt-ended with Klenow DNA polymerase. The HCV reporter retroviral vector pLNL-Pur-HCV (FIG. 9D) is constructed by purifying the 2065 bp PvuII/XbaI fragment from pPur-HCV, which contains the SV40 early promoter, the puromycin resistance coding region and the HCV 5'UTR and capsid sequences. The fragment is blunt-ended with Klenow and cloned into plasmid pLNL6 (Bender et al., J. Virol. 61:1639-1646, 1987; FIG. 9C) that has been digested with HindIII and blunt-ended with Klenow. Both resulting HCV reporter plasmids will then produce an RNA transcript, via SV40 early promoter, that contains the HCV 5' UTR and capsid sequences on the same RNA transcript as the coding region for puromycin resistance. Each HCV ribozyme is expressed on a separate retroviral vector (pLNT-Rz) via the tRNA.sup.val pol III promoter. Active HCV ribozymes will cleave the Pur-HCV RNA, resulting in a cell sensitive to puromycin.

DEPR:
Briefly, HeLa or HT1080 cells are co-transfected with pPur-HCV and various pLNT-Rz constructs

using standard calcium phosphate methods. DNA molar ratios for the HCV:Rz co-transfections is
1:10, using empty pLNT vector to maintain total DNA at 20 .mu.g. Ribozymes tested included two
anti-HCV ribozymes: CR2 (against the 5' UTR) and CR4 (against capsid), and one disabled anti-HBV
ribozyme, dBR1, included as a negative control. Cells are selected with 1 .mu.g/ml puromycin
starting 24 hours post transfection, and continued for up to two weeks. Puromycin-resistant
colonies are visualized by crystal violet staining and counted. Ribozyme expression within the
transfected cells is verified by RNase protection. Using radiolabeled antisense CR4 RNA as the
RNase protection probe, the expected protected fragments are 64 nt for CR4, 42 nt for CR2 and 32
nt for dCR4 (FIG. 10; RNase Protection Assay Kit is available from Promega, Madison, Wis.).

DEPR:
CR4 Rz activity in reducing HCV gene expression was tested in tissue culture. Briefly, CR4
Ribozyme was expressed from pAvC-CR4 described in Example 9. Western blot to detect HCV core
antigen was used to evaluate the effectiveness of ribozyme in inhibiting the intracellular
synthesis of HCV capsid in tissue culture. In particular, HT1080 cells were co-transfected by
pPur-HCV (see FIG. 23) and pAvC-CR4 at a molar ratio of 1:10 of 1:20 using method described in
Example 5. Ribozymes tested included CR4 and disabled CR4 (dCR4). Cells were harvested at 24
hours post transfection and processed for HCV core Western blot.

6. Document ID: US 5939538 A

L8: Entry 6 of 18 File: USPT Aug 17, 1999

US-PAT-NO: 5939538
DOCUMENT-IDENTIFIER: US 5939538 A
TITLE: Methods and compositions for inhibiting HIV infection of cells by cleaving HIV co-receptor
RNA
DATE-ISSUED: August 17, 1999

US-CL-CURRENT: 536/23.1

APPL-NO: 8/ 770235
DATE FILED: December 19, 1996

PARENT-CASE:
This application claims priority to provisional application Ser. No. 60/027,875, filed Oct. 25,
1996, now abandoned.

IN: Leavitt; Markley C., Tritz; Richard, Feng; Yu, Barber; Jack, Yu; Mang

AB: Methods of inhibiting HIV infection by blocking HIV co-receptor RNA expression
are provided. Ribozymes which cleave HIV co-receptor RNA and inhibit HIV infection of cells
are also provided. Co-receptor targets include fusin and CKR5.

L8: Entry 6 of 18 File: USPT Aug 17, 1999

DOCUMENT-IDENTIFIER: US 5939538 A
TITLE: Methods and compositions for inhibiting HIV infection of cells by cleaving HIV co-receptor
RNA

DEPR:
In one class of embodiments, the vector is replicated and packaged into HIV capsids using the HIV
replication machinery, thereby causing the anti-HIV ribozyme to propagate in conjunction with the
replication of an HIV virus. Thus, an organism infected with HIV can be treated for the infection
by transducing a population of its cells with a vector of the invention and introducing the
transduced cells back into the organism as described herein. Thus, the present invention provides
compositions and methods for protecting cells in culture, ex vivo and in a patient.

7. Document ID: US 5853716 A

L8: Entry 7 of 18 File: USPT Dec 29, 1998

US-PAT-NO: 5853716
DOCUMENT-IDENTIFIER: US 5853716 A
TITLE: Genetically engineered chimeric viruses for the treatment of diseases associated with
viral transactivators
DATE-ISSUED: December 29, 1998

US-CL-CURRENT: 424/93.2; 424/93.6, 435/357, 435/372.3, 536/24.1

APPL-NO: 8/ 690174
DATE FILED: July 25, 1996

IN: Tattersall; Peter J., Cotmore; Susan F.

AB: The present invention relates to chimeric viruses, the replication of which is
regulated by a transactivation signal produced by diseased host cells. The chimeric viruses
of the invention can infect both normal and diseased host cells. However, the chimeric virus
replicates efficiently in and kills diseased host cells that produce the transactivation
signal. The use of such chimeric viruses to treat infectious diseases and cancers are
described. A particularly useful embodiment involves the modification of a murine parvovirus
that infects human T cells to generate a chimeric parvovirus that is cytocidal to human T
cells that express HIV-tat. The chimeric parvovirus can be used to treat HIV-infection.

L8: Entry 7 of 18 File: USPT Dec 29, 1998

DOCUMENT-IDENTIFIER: US 5853716 A
TITLE: Genetically engineered chimeric viruses for the treatment of diseases associated with
viral transactivators

DEPR:
The invention also encompasses a nucleotide sequence encoding a ribozyme that cleaves the HIV-tat
mRNA and prevents its translation, to be inserted in place of the complementable capsid gene of
parvovirus. Within the scope of the invention are engineered hammerhead motif ribozyme molecules
that specifically and efficiently catalyze endonucleolytic cleavage of HIV-tat or other
transactivating factor transcripts. Specific ribozyme cleavage sites within any potential RNA
target are initially identified by scanning the target molecule for ribozyme cleavage sites which
include the following sequences, GUA, GUU, and GUC. Once identified, short RNA sequences of
between 15 and 20 ribonucleotides corresponding to the region of the HIV-tat coding sequence
containing the cleavage site may be evaluated for predicted structural features such as secondary
structure that may render the oligonucleotide sequence unsuitable.

8. Document ID: US 5849891 A

L8: Entry 8 of 18

File: USPT

Dec 15, 1998

US-PAT-NO: 5849891
DOCUMENT-IDENTIFIER: US 5849891 A
TITLE: Satellite RNA from bamboo mosaic virus as a vector for foreign gene expression in plants
DATE-ISSUED: December 15, 1998

US-CL-CURRENT: 536/23.1; 435/320.1, 435/5

APPL-NO: 8/ 511717
DATE FILED: July 28, 1995

IN: Lin; Na-Sheng, Hsu; Yau-Heiu

AB: A satellite RNA was found to be naturally associated with bamboo mosaic virus
(BaMV-V) isolated from infected Bambusa vulgaris McClure. Nucleotide sequence revealed that
this satellite RNA genome contains 836 nucleotides and encodes a 20 kDa protein. Infectious
transcripts have been generated from full length cDNA downstream T7 RNA polymerase promoter.
Precise replacement of open reading frame (ORF) of cDNA of satellite RNA with sequence
encoding bacterial CAT (chloramphenicol acetyltransferase) resulted in high level expression
of CAT in infected dicotyledon plants, Chenopodium quinoa and tobacco (Nicotiana
benthamiana) in the presence of baMV genomic RNA. Thus, this satellite system is potentially
useful as a satellite-based plant expression vector.

L8: Entry 8 of 18

File: USPT

Dec 15, 1998

DOCUMENT-IDENTIFIER: US 5849891 A
TITLE: Satellite RNA from bamboo mosaic virus as a vector for foreign gene expression in plants

BSPR:
Still one more aspect of the present invention is to provide for a plant expression system for
the production of biologically active or pharmaceutically important polypeptides. In addition to
bacterial reporter gene CAT, the sBaMV vector in this invention can also successfully express the
3A movement protein of CMV in the infected cells in our laboratories. Thus, any potential or
interested genes can be expressed in the plants through this vector. For example, the ribozyme
containing the sequence specific to BaMV capsid protein can be developed to reduce disease caused
by BaMV; the surface antigen of Heptatis B virus can be produced in plants as clinical vaccine;
and all other pharmaceutical enzymes, polypetides, or proteins can be potentially expressed to
change amino acid contents in plants.

9. Document ID: US 5837854 A

L8: Entry 9 of 18

File: USPT

Nov 17, 1998

US-PAT-NO: 5837854
DOCUMENT-IDENTIFIER: US 5837854 A
TITLE: Oligonucleotides with anti-Epstein-Barr virus activity
DATE-ISSUED: November 17, 1998

US-CL-CURRENT: 536/24.5; 435/238, 435/375

APPL-NO: 8/ 628422
DATE FILED: April 5, 1996

IN: Mulder; Carel

AB: Oligonucleotides that inhibit Epstein-Barr virus functions, pharmaceutical
compositions containing such oligonucleotides, and methods of using these compositions to
treat Epstein-Barr virus-associated diseases.

L8: Entry 9 of 18

File: USPT

Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837854 A
TITLE: Oligonucleotides with anti-Epstein-Barr virus activity

DRPR:
FIG. 3A is a graph showing the levels of expression of the EBV Late gene viral Capsid Antigen
(VCA) after induction of the EBV lytic cycle in Akata cells treated with various concentrations
of PS control (-.smallcircle.-) or PS BZLF1 antisense (-.circle-solid.-) oligonucleotides.

10. Document ID: US 5741706 A

L8: Entry 10 of 18

File: USPT

Apr 21, 1998

US-PAT-NO: 5741706
DOCUMENT-IDENTIFIER: US 5741706 A
TITLE: Anti-HIV ribozymes
DATE-ISSUED: April 21, 1998

US-CL-CURRENT: 435/372; 435/320.1, 435/325, 435/366, 435/6, 435/91.31, 536/23.1, 536/23.2, 536/24.5

APPL-NO: 8/ 719593
DATE FILED: September 25, 1996

IN: Leavitt; Markley C., Tritz; Richard, Duarte; Elizabeth, Barber; Jack, Yu; Mang

AB: GUC and GUA ribozymes which cleave HIV RNA are provided. The ribozymes cleave HIV RNA in vitro and in vivo. When the ribozymes are expressed in cells, they inhibit HIV replication in the cells.

L8: Entry 10 of 18

File: USPT

Apr 21, 1998

DOCUMENT-IDENTIFIER: US 5741706 A
TITLE: Anti-HIV ribozymes

DEPR:
The ribozymes of the invention inhibit viral replication in cells already infected with HIV virus, in addition to conferring a protective effect to cells which are not infected by HIV. In addition, in one class of embodiments, the vector is replicated and packaged into HIV capsids using the HIV replication machinery, thereby causing the anti-HIV ribozyme to propagate in conjunction with the replication of an HIV virus. Thus, an organism infected with HIV can be treated for the infection by transducing a population of its cells with a vector of the invention and introducing the transduced cells back into the organism as described herein. Thus, the present invention provides compositions and methods for protecting cells in culture, ex vivo and in a patient, even when the cells are already infected with the virus against which protection is sought.

11. Document ID: US 5646034 A

L8: Entry 11 of 18

File: USPT

Jul 8, 1997

US-PAT-NO: 5646034
DOCUMENT-IDENTIFIER: US 5646034 A
TITLE: Increasing rAAV titer
DATE-ISSUED: July 8, 1997

US-CL-CURRENT: 435/325; 435/320.1, 435/457, 435/91.4

APPL-NO: 8/ 487080
DATE FILED: June 7, 1995

IN: Mamounas; Michael, Wong-Staal; Flossie, Leavitt; Mark, Yu; Mang

AB: Methods, kits and compositions for increasing the titer of rAAV vectors are provided.

L8: Entry 11 of 18

File: USPT

Jul 8, 1997

DOCUMENT-IDENTIFIER: US 5646034 A
TITLE: Increasing rAAV titer

BSPR:
In one preferred class of embodiments, the present invention provides methods for producing high titers of rAAV vectors. In the first step of the methods, a recombinant encapsidatable AAV nucleic acid (a rAAV nucleic acid) and a recombinant AAV helper nucleic acid are bound to an AAV helper virus, most typically in the presence of a nucleic acid binding molecule such as a polycation (e.g., poly-1-lysine). The rAAV nucleic acid typically encodes a nucleic acid of interest, such as a gene therapeutic agent (e.g. an anti-HIV or other anti-viral therapeutic agent such as a ribozyme, antisense gene, suicide gene or transdominant gene), as well as AAV cis-sequences necessary for packaging the nucleic acid into an AAV capsid (e.g., the AAV ITR sequences). The helper nucleic acid typically encodes AAV nucleic acids and proteins necessary for encapsidation of the rAAV nucleic acid. In preferred embodiments, the helper nucleic acid does not encode sequences necessary for encapsidating itself into a viral capsid. For instance, in one embodiment, the helper nucleic acid lacks AAV ITR sequences (an example of such a nucleic acid is the plasmid AD8). Thus, in one embodiment, the rAAV nucleic acid and the helper nucleic acid are non-homologous, and no wild-type AAV virus is produced upon expression and replication of the rAAV and helper nucleic acids in a cell. The AAV helper virus is a virus which allows replication of AAV (and rAAV vectors), such as an adenovirus or herpes virus. In one embodiment, the helper virus is replication defective. Typically, where the helper virus is replication defective, the cell is infected with a replication competent helper virus, often at the time of transfection.

BSPR:
In one class of embodiments, methods of integrating a target nucleic acid into a cellular genome are provided. In the first step, a recombinant AAV (rAAV) nucleic acid and an AAV helper nucleic acid are bound to an AAV helper virus, producing a bound AAV helper virus, most typically in the presence of a nucleic acid binding molecule such as a polycation (e.g., poly-1-lysine). The recombinant rAAV nucleic acid typically encodes a nucleic acid of interest, such as a polypeptide, antisense gene, or ribozyme as well as AAV cis-active sequences necessary for packaging the nucleic acid into an AAV capsid (e.g., the AAV ITR sequences). The AAV helper nucleic acid typically encodes AAV nucleic acids and proteins which operate in trans to encapsidate the rAAV nucleic acid into an AAV capsid. These trans-active sequences include, e.g., the AAV replicase and capsid genes. In preferred embodiments, the helper nucleic acid does not

encode sequences necessary for encapsidating the nucleic acid into a viral capsid. For instance,
in one embodiment, the AAV helper nucleic acid lacks AAV ITR sequences (an example of such a
nucleic acid is the plasmid AD8 described herein). Thus, in one embodiment, the rAAV nucleic acid
and the AAV helper nucleic acid are non-homologous, and no wild-type AAV virus is produced upon
expression and replication of the rAAV and AAV helper nucleic acids in a cell. The AAV helper
virus is a virus which allows replication of AAV and rAAV, such as an adenovirus or herpes virus.
In one embodiment, the helper virus is replication defective. Typically, where the helper virus
is replication defective, the cell is infected with a replication competent helper virus,
generally at the same time as the transfection with the rAAV and helper nucleic acids.

12. Document ID: US 5550047 A

L8: Entry 12 of 18

File: USPT

Aug 27, 1996

US-PAT-NO: 5550047
DOCUMENT-IDENTIFIER: US 5550047 A
TITLE: Oligonucleotides with anti-Epstein-Barr virus activity
DATE-ISSUED: August 27, 1996

US-CL-CURRENT: 435/238; 514/44, 536/23.1, 536/23.72, 536/24.5

APPL-NO: 8/ 199510
DATE FILED: February 18, 1994

IN: Mulder; Carel

AB: Disclosed are oligonucleotides complementary to and hybridizable with a portion
of the BZLF1 RNA of Epstein-Barr virus, useful for inhibiting the induction of the lytic
cycle in EBV-infected cells, and in inhibiting EBV replication.

L8: Entry 12 of 18

File: USPT

Aug 27, 1996

DOCUMENT-IDENTIFIER: US 5550047 A
TITLE: Oligonucleotides with anti-Epstein-Barr virus activity

DEPR:
Yet another way to measure the ability of the antisense oligonucleotides of the invention to
inhibit EBV replication is to measure the presence of the late gene product viral capsid antigen
(VCA), the major capsid protein. Using the same Akata cells treated as described above, slides
were made, frozen, and stained for VCA using fluorescently labelled antibody to VCA. The
percentage of VCA-positive cells are then counted and plotted versus the oligonucleotide
concentration used.

13. Document ID: WO 9717456 A1

L8: Entry 13 of 18

File: EPAB

May 15, 1997

PUB-NO: WO009717456A1
DOCUMENT-IDENTIFIER: WO 9717456 A1
TITLE: IN VITRO CONSTRUCTION OF SV40 VIRUSES AND PSEUDOVIRUSES

PUBN-DATE: May 15, 1997

INT-CL (IPC): C12N 15/86; C12N 15/87; C12N 15/37; C12N 7/04; C12N 5/10; C07K 14/025; A61K 39/12;
A61K 48/00

APPL-NO: IL09600143
APPL-DATE: November 6, 1996

PRIORITY-DATA:

IN: SANDALON, ZIV, OPPENHEIM, AMOS B, OPPENHEIM, ARIELLA

AB: The invention relates to constructs capable of infecting mammalian cells
comprising at least one semi-purified or pure SV40 capsid protein and a constituent selected
from the group consisting of an exogenous DNA, a vector comprising an exogenous DNA, an
exogenous RNA, a vector comprising an exogenous RNA, an exogenous protein or peptide
product, and antisense RNA, ribozyme RNA or any RNA or DNA which inhibits or prevents the
expression of undesired protein(s) in said mammalian cell and optionally further comprising
operatively linked regulatory elements sufficient for the expression and/or replication of
said exogenous protein in a mammalian cell. The protein product is preferably a therapeutic
protein or peptide product which is not made or contained in mammalian cells, or is made or
contained in such cells in abnormally low amount, or is made or contained in such cells in
defective form, or is made or contained in mammalian cells in physiologically abnormal or
normal amount and can be an enzyme, a receptor, a structural protein, a regulatory protein
or a hormone. The invention further relates to a method for the in vitro construction of
SV40 viruses or pseudoviruses constructs according to the invention. In a further aspect,
the invention relates to mammalian, preferably human cells infected with the constructs of
the invention or with constructs obtained by any of the methods of the invention. Still
further, the invention relates to a method of providing a therapeutic DNA, RNA, protein or
peptide product or antisense RNA to a patient in need of such product by administering to
the patient a therapeutically effective amount of the SV40 viruses or pseudoviruses of the
invention or a therapeutically effective amount of infected cells according to the
invention. Pharmaceutical compositions comprising as active ingredient a therapeutically
effective amount of the SV40 viruses or pseudoviruses according to the invention or a
therapeutically effective amount of infected cells according to the invention are also
within scope of this application.

L8: Entry 13 of 18

File: EPAB

May 15, 1997

DOCUMENT-IDENTIFIER: WO 9717456 A1
TITLE: IN VITRO CONSTRUCTION OF SV40 VIRUSES AND PSEUDOVIRUSES

FPAR:
The invention relates to constructs capable of infecting mammalian cells comprising at least one semi-purified or pure SV40 capsid protein and a constituent selected from the group consisting of an exogenous DNA, a vector comprising an exogenous DNA, an exogenous RNA, a vector comprising an exogenous RNA, an exogenous protein or peptide product, and antisense RNA, ribozyme RNA or any RNA or DNA which inhibits or prevents the expression of undesired protein(s) in said mammalian cell and optionally further comprising operatively linked regulatory elements sufficient for the expression and/or replication of said exogenous protein in a mammalian cell. The protein product is preferably a therapeutic protein or peptide product which is not made or contained in mammalian cells, or is made or contained in such cells in abnormally low amount, or is made or contained in such cells in defective form, or is made or contained in mammalian cells in physiologically abnormal or normal amount and can be an enzyme, a receptor, a structural protein, a regulatory protein or a hormone. The invention further relates to a method for the in vitro construction of SV40 viruses or pseudoviruses constructs according to the invention. In a further aspect, the invention relates to mammalian, preferably human cells infected with the constructs of the invention or with constructs obtained by any of the methods of the invention. Still further, the invention relates to a method of providing a therapeutic DNA, RNA, protein or peptide product or antisense RNA to a patient in need of such product by administering to the patient a therapeutically effective amount of the SV40 viruses or pseudoviruses of the invention or a therapeutically effective amount of infected cells according to the invention.
Pharmaceutical compositions comprising as active ingredient a therapeutically effective amount of the SV40 viruses or pseudoviruses according to the invention or a therapeutically effective amount of infected cells according to the invention are also within scope of this application.

14. Document ID: US 5739310 A, WO 9740060 A1, AU 9727358 A

L8: Entry 14 of 18

File: DWPI

Apr 14, 1998

DERWENT-ACC-NO: 1997-535771
DERWENT-WEEK: 199822

TITLE: Ribosomal vectors containing heterologous DNA in the expansion segment - useful to selectively inhibit expression of a targeted gene in transformed cells, e.g. for gene therapy, virus inhibition and plant engineering

PRIORITY-DATA: 1996US-0639256 (April 23, 1996)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5739310 A	April 14, 1998	N/A	014	C07H021/04
WO 9740060 A1	October 30, 1997	E	040	C07H021/04
AU 9727358 A	November 12, 1997	N/A	000	C07H021/04

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
US 5739310A	April 23, 1996	1996US-0639256	N/A
WO 9740060A1	April 17, 1997	1997WO-US06543	N/A
AU 9727358A	April 17, 1997	1997AU-0027358	N/A
AU 9727358A		WO 9740060	Based on

INT-CL (IPC): C07H 21/04; C12N 1/00; C12N 15/63; C12N 15/74; C12N 15/79; C12N 15/85

IN: FAN, Q, SWEENEY, R, YAO, M

AB: A vector comprising a ribosomal DNA (rDNA) sequence containing an expansion segment with a transcribable heterologous DNA sequence inserted within it is new. Also claimed are host cells containing the vector., USE - The rDNA vector can be used as a vehicle for heterologous sequences to selectively inhibit targeted gene expression in a host cell, by introducing it into the cell and transcribing the heterologous DNA into RNA, which inhibits expression of the targeted gene (claimed). Vectors comprising large or small subunit RNA genes and/or heterologous sequences encoding antisense or ribozyme sequences specific for a transcription product of the targeted gene are especially useful (claimed), particularly if the vector is packaged in a viral capsid or liposome (claimed). The vectors are useful in therapeutic inhibition of gene expression (e.g. genes encoding defective products, oncogenes, viruses etc.), plant engineering (e.g. regulation of fruit softening or viruses) and inhibiting RNA protein binding sites (e.g. for the Rev protein to inhibit HIV replication). They can also be used to treat pathological states e.g. restenosis, leukaemia

etc., to generate transgenic animals and to correlate nucleotide sequences with particular
phenotypes, by generating antisense sequences from a host cell genome, inserting these into
the vector to generate a library and introducing this into host cells which are observed for
the phenotype., A vector comprising a ribosomal DNA (rDNA) sequence containing an expansion
segment with a transcribable heterologous DNA sequence inserted within it is new. Also
claimed are host cells containing the vector., USE - The rDNA vector can be used as a
vehicle for heterologous sequences to selectively inhibit targeted gene expression in a host
cell, by introducing it into the cell and transcribing the heterologous DNA into RNA, which
inhibits expression of the targeted gene (claimed). Vectors comprising large or small
subunit RNA genes and/or heterologous sequences encoding antisense or ribozyme sequences
specific for a transcription product of the targeted gene are especially useful (claimed),
particularly if the vector is packaged in a viral capsid or liposome (claimed). The vectors
are useful in therapeutic inhibition of gene expression (e.g. genes encoding defective
products, oncogenes, viruses etc.), plant engineering (e.g. regulation of fruit softening or
viruses) and inhibiting RNA protein binding sites (e.g. for the Rev protein to inhibit HIV
replication). They can also be used to treat pathological states e.g. restenosis, leukaemia
etc., to generate transgenic animals and to correlate nucleotide sequences with particular
phenotypes, by generating antisense sequences from a host cell genome, inserting these into
the vector to generate a library and introducing this into host cells which are observed for
the phenotype.

L8: Entry 14 of 18

File: DWPI

Apr 14, 1998

DERWENT-ACC-NO: 1997-535771
DERWENT-WEEK: 199822

TITLE: Ribosomal vectors containing heterologous DNA in the expansion segment - useful to
selectively inhibit expression of a targeted gene in transformed cells, e.g. for gene therapy,
virus inhibition and plant engineering

ABTX:
USE - The rDNA vector can be used as a vehicle for heterologous sequences to selectively inhibit
targeted gene expression in a host cell, by introducing it into the cell and transcribing the
heterologous DNA into RNA, which inhibits expression of the targeted gene (claimed). Vectors
comprising large or small subunit RNA genes and/or heterologous sequences encoding antisense or
ribozyme sequences specific for a transcription product of the targeted gene are especially
useful (claimed), particularly if the vector is packaged in a viral capsid or liposome (claimed).
The vectors are useful in therapeutic inhibition of gene expression (e.g. genes encoding
defective products, oncogenes, viruses etc.), plant engineering (e.g. regulation of fruit
softening or viruses) and inhibiting RNA protein binding sites (e.g. for the Rev protein to
inhibit HIV replication). They can also be used to treat pathological states e.g. restenosis,
leukaemia etc., to generate transgenic animals and to correlate nucleotide sequences with
particular phenotypes, by generating antisense sequences from a host cell genome, inserting these
into the vector to generate a library and introducing this into host cells which are observed for
the phenotype.

ABEQ:
USE - The rDNA vector can be used as a vehicle for heterologous sequences to selectively inhibit
targeted gene expression in a host cell, by introducing it into the cell and transcribing the
heterologous DNA into RNA, which inhibits expression of the targeted gene (claimed). Vectors
comprising large or small subunit RNA genes and/or heterologous sequences encoding antisense or
ribozyme sequences specific for a transcription product of the targeted gene are especially
useful (claimed), particularly if the vector is packaged in a viral capsid or liposome (claimed).
The vectors are useful in therapeutic inhibition of gene expression (e.g. genes encoding
defective products, oncogenes, viruses etc.), plant engineering (e.g. regulation of fruit
softening or viruses) and inhibiting RNA protein binding sites (e.g. for the Rev protein to
inhibit HIV replication). They can also be used to treat pathological states e.g. restenosis,
leukaemia etc., to generate transgenic animals and to correlate nucleotide sequences with
particular phenotypes, by generating antisense sequences from a host cell genome, inserting these
into the vector to generate a library and introducing this into host cells which are observed for
the phenotype.

15. Document ID: JP 2000500973 W, DE 19543553 A1, WO 9719174 A1, EP 862633 A1

L8: Entry 15 of 18

File: DWPI

Feb 2, 2000

DERWENT-ACC-NO: 1997-290327
DERWENT-WEEK: 200017

TITLE: Virus-like particle comprising several molecules of JC virus protein VP1 - for diagnosis
or therapy of progressive multifocal leuko:encephalopathy

PRIORITY-DATA: 1995DE-1043553 (November 22, 1995)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2000500973 W	February 2, 2000	N/A	037	C12N015/09
DE 19543553 A1	May 28, 1997	N/A	012	C07K014/025
WO 9719174 A1	May 29, 1997	G		

038
C12N015/37
EP 862633 A1
September 9, 1998
G
000
C12N015/37

APPLICATION-DATA:
PUB-NO
APPL-DATE
APPL-NO
DESCRIPTOR
JP2000500973W
November 22, 1996
1996WO-EP05177
N/A
JP2000500973W
November 22, 1996
1997JP-0519407
N/A
JP2000500973W
WO 9719174
Based on
DE 19543553A1
November 22, 1995
1995DE-1043553
N/A
WO 9719174A1
November 22, 1996
1996WO-EP05177
N/A
EP 862633A1
November 22, 1996
1996EP-0941013
N/A
EP 862633A1
November 22, 1996
1996WO-EP05177
N/A
EP 862633A1
WO 9719174
Based on

INT-CL (IPC): A61K 31/70; A61K 38/00; A61K 38/16; A61K 39/12; A61K 48/00; A61P 25/04; A61P 31/12; C07K 14/025; C07K 14/16; C12N 5/10; C12N 7/00; C12N 15/09; C12N 15/37; C12N 15/79; C12N 15/85; C12P 21/02; C12Q 1/70; G01N 33/53; G01N 33/569; C12N 15/09; C12P 21/02; C12R 1/19; C12R 1/92

IN: HUNSMANN, G, LUEKE, W, WEBER, T

AB: A virus-like particle (VLP) comprising several molecules of the JC virus protein VP1 is new. Also claimed are: (1) a nucleic acid sequence that encodes VP1 protein which comprises: (a) a 1121 bp DNA sequence (given in the specification); (b) a sequence as in (a) which differs due to the degeneracy of the genetic code; and (c) sequences that hybridise with (a) or (b) under stringent hybridisation conditions; (2) a recombinant vector containing at least one copy of the DNA under the control of an expression signal; and (3) cells transformed with the vector., USE - The VLP is useful for detecting antibodies to JC virus by immunoassay, especially for diagnosis of progressive multifocal leukoencephalopathy (PML) by assaying cerebrospinal fluid and serum samples from the same patient. The VLP can be used for therapy of PML and as a transport vehicle, preferably for an antisense nucleic acid (especially a tumour necrosis factor alpha antisense nucleic acid) included within its capsid envelope.

L8: Entry 15 of 18
File: DWPI
Feb 2, 2000

DERWENT-ACC-NO: 1997-290327
DERWENT-WEEK: 200017

TITLE: Virus-like particle comprising several molecules of JC virus protein VP1 - for diagnosis or therapy of progressive multifocal leuko:encephalopathy

ABTX:
USE - The VLP is useful for detecting antibodies to JC virus by immunoassay, especially for diagnosis of progressive multifocal leukoencephalopathy (PML) by assaying cerebrospinal fluid and serum samples from the same patient. The VLP can be used for therapy of PML and as a transport vehicle, preferably for an antisense nucleic acid (especially a tumour necrosis factor alpha antisense nucleic acid) included within its capsid envelope.

16. Document ID: AU 719601 B, WO 9717456 A1, AU 9673314 A, EP 859855 A1
L8: Entry 16 of 18
File: DWPI
May 11, 2000

DERWENT-ACC-NO: 1997-281045
DERWENT-WEEK: 200031

TITLE: Construct able to infect mammalian cells - contains SV40 capsid protein, exogenous nucleic acid, vector or protein, used in gene and replacement therapy of e.g. thalassemia, AIDS or leukaemia

PRIORITY-DATA: 1995IL-0115880 (November 6, 1995)

PATENT-FAMILY:
PUB-NO
PUB-DATE
LANGUAGE
PAGES
MAIN-IPC
AU 719601 B
May 11, 2000
N/A
000
C12N015/86
WO 9717456 A1
May 15, 1997
E
053
C12N015/86
AU 9673314 A
May 29, 1997
N/A
000
C12N015/86
EP 859855 A1
August 26, 1998
E
000
C12N015/86

APPLICATION-DATA:
PUB-NO
APPL-DATE
APPL-NO
DESCRIPTOR
AU 719601B
November 6, 1996
1996AU-0073314
N/A
AU 719601B
AU 9673314
Previous Publ.
AU 719601B
WO 9717456
Based on
WO 9717456A1
November 6, 1996
1996WO-IL00143
N/A
AU 9673314A
November 6, 1996
1996AU-0073314
N/A
AU 9673314A
WO 9717456
Based on
EP 859855A1
November 6, 1996
1996EP-0935316
N/A
EP 859855A1
November 6, 1996
1996WO-IL00143
N/A
EP 859855A1
WO 9717456
Based on

INT-CL (IPC): A61K 39/12; A61K 48/00; C07K 14/025; C12N 5/10; C12N 7/04; C12N 15/37; C12N 15/86; C12N 15/87

IN: OPPENHEIM, A, OPPENHEIM, A B, SANDALON, Z

AB: Construct able to infect mammalian cells comprises: (1) at least 1 (semi)pure
SV40 capsid protein (I); (2) 1 of: (a) exogenous DNA (II) encoding protein, peptide of
therapeutic RNA, or being itself a therapeutic product; (b) exogenous RNA (III) encoding a
protein or peptide, or being itself a therapeutic product; (c) a vector containing (II) or
(III); (d) exogenous protein or peptide; (e) antisense or ribozyme RNA, or any RNA or DNA
that inhibits or prevents expression of unwanted protein in the cell, and (3) optionally
regulatory elements for expression and/or replication of the exogenous component., USE - The
construct, or cells infected with them, are used to deliver any of components (2) to
patients. Particular applications are the treatment of beta -thalassemia (provision of beta
-globin), AIDS (HIV-specific ribozyme), chronic myelogenous leukaemia (antisense RNA against
the bcr/abl gene), to accelerate wound healing (transient delivery of fibroblast growth
factor and prevention of haemorrhage/dissolution of thrombi (transient delivery of blood
clotting or anticoagulation agents)., ADVANTAGE - The constructs, which are SV40
(pseudo)viruses, are prepared by in vitro packaging under aseptic conditions which provides
maximum safety since all process steps can be controlled and contamination by recombinants
is avoided. The constructs provide very efficient gene transfer into a wide range of cells
and only 200 bp SV40 DNA is required (not the ses element as needed in in vivo packaging),
although at most 7.5 kb nucleic acid can be cloned, giving products in which > 95% of the
DNA is human. The SV40 proteins can be produced in insect cells while the DNA component can
be made in bacteria and purified before packaging (to minimise chances of selecting
spontaneous mutations or rearrangements). The constructs may include or encode proteins that
promote homologous recombination, so can be used for gene replacement (targeting) therapy.

L8: Entry 16 of 18
File: DWPI
May 11, 2000

DERWENT-ACC-NO: 1997-281045
DERWENT-WEEK: 200031

TITLE: Construct able to infect mammalian cells - contains SV40 capsid protein, exogenous nucleic
acid, vector or protein, used in gene and replacement therapy of e.g. thalassemia, AIDS or
leukaemia

AB TX:
Construct able to infect mammalian cells comprises: (1) at least 1 (semi)pure SV40 capsid protein
(I); (2) 1 of: (a) exogenous DNA (II) encoding protein, peptide of therapeutic RNA, or being
itself a therapeutic product; (b) exogenous RNA (III) encoding a protein or peptide, or being
itself a therapeutic product; (c) a vector containing (II) or (III); (d) exogenous protein or
peptide; (e) antisense or ribozyme RNA, or any RNA or DNA that inhibits or prevents expression of
unwanted protein in the cell, and (3) optionally regulatory elements for expression and/or
replication of the exogenous component.

17. Document ID: US 5607842 A, WO 9408033 A1
L8: Entry 17 of 18
File: DWPI
Mar 4, 1997

DERWENT-ACC-NO: 1994-135593
DERWENT-WEEK: 199715

TITLE: Expression system for prokaryotic hosts - comprises cell unable to produce essential tRNA
and plasmid, contg. structural gene, also providing this tRNA, can be stably maintained without
selection

PRIORITY-DATA: 1992US-0955982 (October 2, 1992), 1994US-0230427 (April 19, 1994)

PATENT-FAMILY:
PUB-NO
PUB-DATE
LANGUAGE
PAGES
MAIN-IPC
US 5607842 A
March 4, 1997
N/A
015

C12P021/02

WO 9408033 A1
April 14, 1994
E
039
C12P021/00

APPLICATION-DATA:
PUB-NO
APPL-DATE
APPL-NO
DESCRIPTOR
US 5607842A
October 2, 1992
1992US-0955982
Cont of
US 5607842A
April 19, 1994
1994US-0230427
N/A
WO 9408033A1
September 22, 1993
1993WO-US09018
N/A

INT-CL (IPC): C12N 1/21; C12N 15/00; C12N 15/11; C12N 15/63; C12N 15/70; C12N 15/74; C12N 15/85; C12P 21/00; C12P 21/02

IN: COHEN, S N, VOGTLI, M

AB: Expression system comprises prokaryotic host able to secrete protein and having a negative background for a tRNA providing a specific amino acid for expression, plus a plasmid having an origin of replication (ori), functional gene for this tRNA and a structural gene of interest., Also new are such plasmids (in which ori is unstably maintained in the host)., Partic., hosts are of the family Actinomycetaceae, esp. the genus Streptomyces, and the amino acid is tyrosine., USE/ADVANTAGE - The hosts are used to express an exogenous protein (I), e.g., a nutrient or drug such as a colony-stimulating factor, interleukin, fibrinogen, growth hormone, enzyme, HIV capsid protein, etc. Also contemplated (not claimed) is prodn. of antisense RNA from the exogenous gene. This system provides safe maintenance of plasmid in the host and vigorous growth and efficient expression of (I) in non-selective medium (since loss of the plasmid will cause death of the host), i.e., the deleterious effect of selection agents is avoided. The tRNA gene does not encode a potentially contaminating protein; does not effect level of expression of other genes, is small and has a low probability of chromosomal integration., A new expression system for producing an exogenous protein in a prokaryotic host, the system comprising:, a secretory prokaryotic host having a negative background for an essential tRNA specific for an amino acid, and, a plasmid having an origin of replication, a functional gene for a tRNA specific for said amino acid, and a structural gene of interest which when present in said host is expressed.

L8: Entry 17 of 18
File: DWPI
Mar 4, 1997

DERWENT-ACC-NO: 1994-135593
DERWENT-WEEK: 199715
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TITLE: Expression system for prokaryotic hosts - comprises cell unable to produce essential tRNA and plasmid, contg. structural gene, also providing this tRNA, can be stably maintained without selection

ABTX:
USE/ADVANTAGE - The hosts are used to express an exogenous protein (I), e.g., a nutrient or drug such as a colony-stimulating factor, interleukin, fibrinogen, growth hormone, enzyme, HIV capsid protein, etc. Also contemplated (not claimed) is prodn. of antisense RNA from the exogenous gene. This system provides safe maintenance of plasmid in the host and vigorous growth and efficient expression of (I) in non-selective medium (since loss of the plasmid will cause death of the host), i.e., the deleterious effect of selection agents is avoided. The tRNA gene does not encode a potentially contaminating protein; does not effect level of expression of other genes, is small and has a low probability of chromosomal integration.

18. Document ID: WO 9322430 A1, AU 9342207 A, EP 652948 A1, JP 08503844 W, AU 672409 B, EP 652948 A4
L8: Entry 18 of 18
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Nov 11, 1993

DERWENT-ACC-NO: 1993-368789
DERWENT-WEEK: 200030
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TITLE: Vector based on keratin gene for selective expression in epidermis - e.g. for stimulating wound healing, treating psoriasis and skin cancer etc., also transformed epidermal cells and transgenic animals

PRIORITY-DATA: 1992US-0876289 (April 30, 1992)

PATENT-FAMILY:
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1993WO-US03985
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AU 9342207A
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IN: GREENHALGH, D A, ROOP, D R, ROTHNAGEL, J A, YUSPA, S H

AB: Keratin K1 vector for expressing a nucleic acid cassette in the epidermis
comprises (1) a 5'-flanking region of the keratin K1 gene, including the K1 promoter,
5'-transcribed (but untranslated) region and a first intron, all in sequence and position
for expression; (2) a 3'-flanking region of the K1 gene contg. vitamin D3 regulatory
sequences, including a 3'-transcribed (but not translated) region and contiguous non-coding
DNA contg. the transcription termination region; and (3) a polylinker, which connects the
5'- and 3'-flanking regions and provides a position for insertion of the specified
cassette., Also new are (1) bioreactors contg. epidermal cells transfected with this vector;
(2) a noncoding fragment of the human K1 gene contg. regulatory sequences; and (3)
transgenic animals contg. the new vectors., USE/ADVANTAGE - Transgenic animals carrying an
oncogene are useful for studying origin and treatment of cancer. The vectors can be used for
in vivo transduction of human epidermal cells esp. for (1) stimulating healing of wounds,
surgical incisions or ulcers (where the vector expresses a growth factor); (2) treating
psoriasis (the vector expresses transforming growth factor beta, a soluble cytokine receptor
or antisense RNA); (3) treating skin cancer (the vector expresses antisense RNA of the E6 or
E7 gene of human papilloma virus or normal p53 protein); (4) for vaccination (the vector
expresses a viral capsid protein, esp. of human papilloma virus). Alternatively human
epidermal cells are transduced ex vivo, then transplanted.

L8: Entry 18 of 18
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Nov 11, 1993

DERWENT-ACC-NO: 1993-368789
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TITLE: Vector based on keratin gene for selective expression in epidermis - e.g. for stimulating
wound healing, treating psoriasis and skin cancer etc., also transformed epidermal cells and
transgenic animals

ABTX:
USE/ADVANTAGE - Transgenic animals carrying an oncogene are useful for studying origin and
treatment of cancer. The vectors can be used for in vivo transduction of human epidermal cells
esp. for (1) stimulating healing of wounds, surgical incisions or ulcers (where the vector
expresses a growth factor); (2) treating psoriasis (the vector expresses transforming growth
factor beta, a soluble cytokine receptor or antisense RNA); (3) treating skin cancer (the vector
expresses antisense RNA of the E6 or E7 gene of human papilloma virus or normal p53 protein); (4)
for vaccination (the vector expresses a viral capsid protein, esp. of human papilloma virus).
Alternatively human epidermal cells are transduced ex vivo, then transplanted.